

Claims

1. A liposome, wherein cholesterol (CH) and sphingomyelin (SM) are present in relation to the total molar lipid composition of the liposome at a molar ratio of 30 to 60 mol% and 5 to 20 mol%, respectively.
2. The liposome of claim 1, wherein SM is present in relation to the total molar lipid composition of the liposome at a molar ratio of 10 to 18 mol%, in particular 12 to 16 mol%.
3. The liposome of claim 1 or 2, wherein CH is present in relation to the total molar lipid composition of the liposome at a molar ratio of 40 to 56 mol%, in particular 48 to 52 mol%.
4. The liposome of one of claims 1 to 3, wherein the remaining lipid of the liposome is selected from the group consisting of glycerides, glycerophospholipides, glycerophosphinolipids, glycerophosphonolipids, sulfolipids, sphingolipids, phospholipids, isoprenolides, steroids, stearines, sterols and carbohydrate containing lipids.
5. The liposome of claim 4, wherein the phospholipid is selected from the group consisting of phosphatidylcholine (PC), phosphatidylserine (PS), and phosphatidylethanolamine (PE).
6. The liposome of claim 5, wherein the PE is present in relation to the total molar lipid composition of the liposome at a molar ratio of 5 to 25 mol%.
7. The liposome of claim 5 or 6, wherein the PC is present in relation to the total molar lipid composition of the liposome at a molar ratio of 15 to 40 mol%.
8. The liposome of one of claims 1 to 7, wherein the liposome has a diameter of between 50 and 200 nm, preferably between 80 and 150 nm.

9. The liposome of one of claims 1 to 8, wherein the SM is selected from the group consisting of SM derived from milk, SM derived from egg yolk, SM derived from brain, and synthetic SM.
- 5 10. The liposome of one of claims 1 to 9, wherein the PE is selected from the group consisting of PE derived from egg; PE derived from heart; PE derived from liver; PE derived from plant; PE derived from bacteria; and synthetic PE, in particular 1,2-diacyl-sn-glycerol-3-PE, 1-acyl-2-acyl-sn-glycerol-3-PE or 1,2-dilauroyl-sn-glycerol-3-PE (DLPE).
- 10 11. The liposome of one of claims 1 to 10, wherein a targeting moiety is attached to the liposome.
12. The liposome of claim 11, wherein the targeting moiety is selected from the group
15 consisting of a peptide or protein, in particular an antibody or fragment thereof, a single-chain antibody or fragment thereof, a receptor ligand or fragment thereof; a carbohydrate; and a ligand.
13. The liposome of one of claim 11, in which the targeting moiety is selected from the
20 group consisting of natural or synthetic receptor-binding peptides, in particular integrin-binding peptides such as RGD-comprising peptides; growth factors, in particular VEGF, EGF, PDGF, TGF α , TGF β , KGF, SDGF, FGF, IGF, HGF, NGF, BDNF, neurotrophine, BMF, bombesin, M-CSF, GM-CSF, thrombopoietin, erythropoietin, SCF, SDGF, oncostatin, PDEGF, endothelin; cytokines, in particular
25 IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-14, IL-15, interferon α , β or γ , tumor necrosis factors such as TNF α , TNF β ; chemokines, in particular RANTES, MCAF, MIP-1 α or β , NAP, β -thromboglobulin; peptide hormones such as SRH, SIH, STH, MRH, MSH, PRH, PIH, prolactin, LH-RH, FSH-RH, LH/ICSH, FSH, TRH, TSH, CRH, ACTH, angiotensin, kinine, histamine; steroid
30 hormones, in particular estrogen, gestagen, androgen, glucocorticoid; mineral corticoids; or homologous or analogous thereof; vitamins, in particular folic acid; adhesion molecules, in particular lewis X, S-lewis X, LFA-1, MAC-1, VLA-4, PECAM, vitronectin, GMP-140, ICAM-1, VCAM-1, fibronectin, laminin, B7, CD28, CD40, CD40L and selectins; viral coatproteins; monosaccharides, in particular

glucose, mannose; and oligosaccharides, in particular Man2, Man3, Man4, Man5, Man6, Man7, Man8, or Man9, lewis Y, sialyl lewis Y, and lectines.

14. The liposome of one of claims 11 to 13, wherein the targeting moiety is attached to a
5 spacer.

15. The liposome of claim 14, wherein the spacer has a length of between 1 and 10 nm, preferably between 2.5 and 5 nm.

10 16. The liposome of one of claims 11 to 15, wherein the targeting moiety is attached to a lipid.

17. The liposome of claim 16, wherein the lipid is selected from the group consisting of
N-caproylamine-PE, N-dodecylamine-PE, phosphatidylthioethanol, N-[4-(p-
15 maleimidomethyl)cyclohexane-carboxamide-PE (N-MCC-PE), N-[4-(p-
maleimidophenyl)butyramide]-PE (N-MPB-PE), N-[3-(2-pyridyldithio)propionate]-PE
(N-PDP-PE), N-succinyl-PE, N-glutaryl-PE, N-dodecanyl-PE, N-biotinyl-PE, N-
biotinyl-Cap-PE, phosphatidyl-(ethylene glycol), PE-polyethylene glycol (PEG)-
carboxylic acid, PE-PEG-maleimide, PE-PEG-PDP, PE-PEG-amine, PE-PEG-biotin,
20 PE-PEG-HNS, dipalmitoyl-glycero succinyl-lysine, alpha-methoxy-omega-(1,2-
dioctadecenoyloxy glyceryl) (DO), and alpha-methoxy-omega-(1,2-
ditetradecenoyloxy glyceryl) (DT).

18. The liposome of one of claims 1 to 17, wherein one or more drugs and/or diagnostics
25 are comprised in the liposome.

19. The liposome of claim 18, wherein the drug is selected from the group consisting of
analgetics, antirheumatics, anthelmintics, antiallergics, antianemics, antiarrhythmics,
antibiotics, antiinfectives, antidementics (nootropics), antidiabetics, antidotes,
30 antiemetics, antivertiginosics, antiepileptics, antihemorrhagics, antihypertensives,
antihypotonics, anticoagulants, antimycotics, antitussiv agents, antiviral agents, beta-
receptor and calcium channel antagonists, broncholytic and antiasthmatic agents,
chemokines, cytokines, mitogens, cytostatics, cytotoxic agents and prodrugs thereof,
dermatics, hypnotics and sedatives, immunosuppressants, immunostimulants, peptide

or protein drugs, in particular hormones and physiological or pharmacological inhibitors of mitogens, chemokines, or cytokines or their respective prodrugs.

20. The liposome of claim 19, wherein the cytostatics and cytotoxic drugs are selected from the group consisting of alkylating substances, anti-metabolites, antibiotics, epothilones, nuclear receptor agonists and antagonists, anti-androgens, anti-estrogens, platinum compounds, hormones and antihormones, interferons and inhibitors of cell cycle-dependent protein kinases (CDKs), inhibitors of cyclooxygenases and/or lipoxygenases, biogenic fatty acids and fatty acid derivatives, including prostanoids and leukotrienes, inhibitors of protein kinases, inhibitors of protein phosphatases, inhibitors of lipid kinases, platinum coordination complexes, ethyleneimines, methylmelamines, trazines, vinca alkaloids, pyrimidine analogs, purine analogs, alkylsulfonates, folic acid analogs, anthracendiones, substituted urea, methylhydrazine derivatives, in particular acediasulfone, aclarubicin, ambazone, aminoglutethimide, L-asparaginase, azathioprine, bleomycin, busulfan, calcium folinate, carboplatin, carpecitabine, carmustine, celecoxib, chlorambucil, cis-platin, cladribine, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, dapsone, daunorubicin, dibrompropamide, diethylstilbestrol, docetaxel, doxorubicin, enedynes, epirubicin, epothilone B, epothilone D, estramucine phosphate, estrogen, ethinylestradiol, etoposide, flavopiridol, floxuridine, fludarabine, fluorouracil, fluoxymesterone, flutamide, fosfestrol, furazolidone, gemcitabine, gonadotropin releasing hormone analog, hexamethylmelamine, hydroxycarbamide, hydroxymethylnitrofurantoin, hydroxyprogesterone caproate, hydroxyurea, idarubicin, idoxuridine, ifosfamide, interferon α , irinotecan, leuprolide, lomustine, lurtotecan, mafenide sulfate, olamide, mechlorethamine, medroxyprogesterone acetate, megestrol acetate, melphalan, mepacrine, mercaptopurine, methotrexate, metronidazole, mitomycin C, mitopodizide, mitotane, mitoxantrone, mithramycin, nalidixic acid, nifuratel, nifuroxazide, nifuralazine, nifurtimox, nimustine, ninorazole, nitrofurantoin, nitrogen mustards, oleomucin, oxolinic acid, pentamidine, pentostatin, phenazopyridine, phthalylsulfathiazole, pipobroman, prednimustine, prednisone, preussin, procarbazine, pyrimethamine, raltitrexed, rapamycin, rofecoxib, rosiglitazone, salazosulfapyridine, scriflavinium chloride, semustine, streptozocine, sulfacarbamide, sulfacetamide, sulfachlopyridazine, sulfadiazine, sulfadiazole, sulfadimethoxine, sulfadithiazole, sulfafurazole, sulfaguanidine, sulfaguanole, sulfamethizole, sulfamethoxazole, co-

trimoxazole, sulfamethoxydiazine, sulfamethoxypyridazine, sulfamoxole, sulfanilamide, sulfaperin, sulfaphenazole, sulfathiazole, sulfisomidine, staurosporin, tamoxifen, taxol, teniposide, tertiposide, testolactone, testosteronepropionate, thioguanine, thiotepa, tinidazole, topotecan, triaziquone, treosulfan, trimethoprim, trofosfamide, UCN-01, vinblastine, vincristine, vindesine, vinblastine, vinorelbine, and zorubicin, or their respective derivatives or analogs thereof.

21. The liposome of claim 18, wherein the diagnostic is selected from the group consisting of an electron dense molecule, a paramagnetic molecule, a superparamagnetic molecule, a radioactive molecule, a non-radioactive isotope, and a fluorescent molecule.

22. The liposome of one of claims 1 to 21, wherein stabilizers, protectants, metal ion chelators, buffers and/or additives are comprised in the liposome.

23. The liposome of one of claims 1 to 22, which is dried, preferably freeze dried.

24. A method for producing a liposome of one of claims 1 to 23, in which SM, CH and remaining lipid(s) are mixed.

25. The method according to claim 24 in which the remaining lipid is selected from PE and PC.

26. A pharmaceutical composition comprising a liposome of one of claims 1 to 23 or produced according to the method of claim 24, further comprising stabilizers, protectants, metal ion chelators, buffers and/or additives.

27. A diagnostic composition comprising a liposome of one of claims 1 to 23 or produced according to the method of claim 24, further comprising stabilizers, protectants, metal ion chelators, buffers and/or additives.

28. The liposome of claim 22 or 23, the pharmaceutical composition of claim 25 or the diagnostic composition of claim 27, wherein the stabilizers are selected from the group consisting of α -tocopherol, vitamin E or carbohydrates, in particular glucose, sorbitol,

sucrose, maltose, trehalose, lactose, cellubiose, raffinose, maltotriose, or dextran.

29. Use of a liposome of one of claims 1 to 23 or a pharmaceutical composition of claim 26 or 28 for the production of a medicament for the therapy of proliferative diseases, autoimmune diseases, infectious diseases, cardiovascular diseases, rheumatoid diseases, inflammatory diseases or any disease or condition, which is associated with damage to or a permeability increase of the vasculature or the activation of endothelial cells.

30. The use of claim 29, wherein the proliferative disease is selected from the group consisting of carcinomas of the gastrointestinal or colorectal tract, liver, pancreas, kidney, bladder, prostate, endometrium, ovary, testes, melanoma, dysplastic oral mucosa, invasive oral cancers, small cell and non-small cell lung carcinomas, hormone-dependent breast cancers, independent breast cancers, transitional and squamous cell cancers, neurological malignancies including neuroblastoma, gliomas, astrocytomas, osteosarcomas, soft tissue sarcomas, hemangioamas, endocrinological tumors, hematologic neoplasias including leukemias, lymphomas, and other myeloproliferative and lymphoproliferative diseases, carcinomas in situ, hyperplastic lesions, adenomas, fibromas, histiocytosis, chronic inflammatory proliferative diseases, vascular proliferative diseases and virus-induced proliferative diseases.

31. Use of a diagnostic composition of claim 27 for the diagnosis of a disease selected from the group of proliferative diseases, autoimmune diseases, infectious diseases, cardiovascular diseases, rheumatoid diseases, and inflammatory diseases.